Gene transfer work awarded U.S. patent

A method for introducing almost any foreign gene into animal cells in laboratory culture so that the transformed cells can be easily recognized has received patent protection. Currently used in basic research, the technique is expected to be useful in commercial production of such biological materials as interferons, blood clotting factors, hormones and vaccines.

The U.S. Patent Office on Aug. 16 issued the patent to Richard Axel and Saul Silverstein of Columbia University in New York, and Michael Wigler of Cold Spring Harbor (N.Y.) Laboratories. Columbia University is offering non-exclusive licensing arrangements with industry.

"Basic scientists are now using these techniques to study the function of normal and mutant genes in a variety of cellular environments," says Axel. "These procedures may also be a prerequisite to the development of a sucessful gene replacement therapy..."

The broad patent covers a technique known to the scientists as "cotransformation." It is based on the observation that cells that take up one type of foreign DNA, probably by engulfing it, are likely to take up another. For example, researchers can introduce a gene for a characteristic that allows the cells containing it to be easily recognized—say, a gene that permits cells to survive under conditions where cells lacking the gene die. If at the same time they expose the cells to another foreign gene, about 80 percent of the easily identified cells containing the first gene also contain the second, Axel says.

Axel and colleagues have demonstrated that the genes introduced with this method attach to the host cell's chromosomes, and the genes may function to make their characteristic proteins in the new environment (SN: 3/6/82, p. 153). The scientists predict that this process will allow the use of animal cells growing in culture for producing biological substances that are now difficult or impossible to make in bacteria.

Axel and colleagues have patent applications that are now pending in Canada, Western Europe, Japan and Australia.

—J.A. Miller

A new predictor for heart disease?

First doctors linked total levels of cholesterol in the blood with heart disease risk. Then they found that the compounds to which cholesterols in the blood are usually attached — high-density lipoproteins (HDL) and low-density lipoproteins (LDL) — were better predictors of heart disease than total serum cholesterol measurements. In other words, if a person had abnormally low levels of HDL-bound cholesterol, or abnormally high levels of LDL-bound cholesterol, he or she was probably at risk of heart disease (SN: 4/22/78, p. 247; 12/4/82, p. 360).

And now it looks as if the major protein component of HDLs may be a still better indicator of heart disease risk than HDL-bound cholesterol. The evidence comes from James J. Maciejko and colleagues at the Mayo Clinic and Foundation in Rochester, Minn.

Maciejko and his co-workers attempted to see whether apolipoprotein A-1, the major protein component of HDLs, was a better indicator of coronary artery disease than was cholesterol bound to HDLs in 108 male subjects. The subjects had come to the Mayo Clinic because of heart disease symptoms. The status of their coronary arteries was checked with the diagnostic test of coronary angiography. Some three-fourths of them were found to have coronary artery disease.

Levels of both HDL-bound cholesterol and apolipoprotein A-1 were found to be significantly lower in diseased subjects than in non-diseased subjects, the researchers report in the Aug. 18 New England Journal of Medicine. However, further analysis revealed that levels of apolipoprotein A-1 discriminated between persons with and without disease better than HDL-bound cholesterol levels.

In an accompanying editorial, Henry Blackburn of the University of Minnesota School of Medicine in Minneapolis concedes that this "almost perfectly predictive association between apolipoprotein A-1 levels and the presence of obstructive coronary-artery disease...induces love at first sight." But "quick romance," he cautions, "does not a marriage make." Is apolipoprotein A-1 truly a better disease indicator than HDL cholesterol, he asks, or might its putative superiority be due to a flaw in study design? "Any diagnostic test or predictive index," he points out, "works better in a population such as that seen at the Mayo Clinic, in which there is a high proportion of cases. A small departure from the perfect specificity of a test, when applied to a general population containing a low proportion of cases, produces many errors."

Yet the more important question, he says, is whether apolipoprotein A-1 might be able to predict future coronary artery disease among the general healthy population. If so, he says, that would be truly exciting. More studies are now underway at the Mayo Clinic to see whether the protein can do so, Maciejko said in an interview. And if the answer is yes, he anticipates apolipoprotein A-1 might eventually replace total cholesterol levels or HDL-bound cholesterol levels as a routine blood screen for heart disease risk.

—J.A. Treichel

Planting the cause of coal ignition

A match's flame, licking at a lump of coal, usually fails to ignite the coal. Yet, coal in underground and open-pit mines or being shipped in railcars and cargo vessels can ignite spontaneously. This spontaneous ignition is a major hazard in the coal industry and a perplexing scientific puzzle.

All types of coal do not have the same tendency to ignite. In the United States, western coal with a relatively low carbon and sulfur content is being mined in increasing amounts for domestic use and for export to Japan. But this coal is more susceptible to spontaneous combustion than other coals. At last week's International Conference on Coal Science, held in Pittsburgh, James R. Herring of the U.S. Geological Survey in Lakewood, Colo., reported new evidence that may explain why this coal is so susceptible. His research could suggest ways of making sure customers don't receive unwanted "hot" coal.

Spontaneous ignition involves the reaction of coal with oxygen by way of a complicated and poorly understood set of chemical reactions. These reactions somehow raise the coal to its ignition temperature of more than 500°C. Observations at strip mines provide clues to the conditions required. Ignition usually occurs where the coal has been disturbed (for example, lying in waste piles at the foot of a coal face) and is near water. This suggests that water and increased surface area exposed to air facilitate heat-generating chemical reactions, Herring said.

Mine operators have also observed that often there are differences in the number of fires in adjacent pits in the same coal seam at a single mine. Herring said, "This seems to suggest that it is not the average properties of the coal that lead to ignition, but rather some minor, subtle differences within the coal itself."

Coal is a complex mixture of organic materials that can be traced back to their individual plant origins. One group of these materials, called exinites, oxidize much more readily and rapidly than the others. Herring said that he suspects that pockets of exinites within coal may serve as centers for heat generation. Both the relative abundance and type of exinite may affect the chances for spontaneous combustion occurring, he said. What isn't clear is why exinites, which contain resin droplets, pollen, spores and other plant remains, react faster.

Whether there is a measurable relationship between exinite content and spontaneous heat generation remains to be determined, said Herring. During the next year, the U.S. Geological Survey will begin a comprehensive sample collection and analysis program to test the hypothesis.

—I. Peterson